Trends in Clinical and Medical Sciences

PSR Press

Original Research Article

A comparative study on the effectiveness of platelet rich plasma injection versus corticosteroid injection in treatment of adhesive capsulitis of shoulder

Pinnaka Vijaya Shankar[1], Thati Bharath[1], Sunkara Rajesh[1,*] and Rangu Aswini[1]

[1] Department of Orthopaedics, ASRAM, Eluru, Andhra Pradesh, India.
* Correspondence: sunkararajesh1996@gmail.com

Received: 25 January 2023; Accepted: 12 May 2023; Published: 27 May 2023.

Abstract: **Objective:** The objective of this study was to compare the effects of single intra-articular platelet-rich plasma (PRP) and corticosteroid (CS) injections in patients diagnosed with adhesive capsulitis of the shoulder.
Design: Patients between the ages of 30-70 years, of either sex, diagnosed with adhesive capsulitis of the shoulder with a duration of less than 6 months, were included. In the intra-articular corticosteroid (IA-CS, control) group, 30 patients received a single injection of IA-CS (2 ml), while in the IA-PRP (test) group, 30 patients received a single IA-PRP injection (2 ml) into the glenohumeral joint under ultrasound guidance. All patients were prospectively followed for 24 weeks.
Results: Thirty patients in the IA-PRP group and thirty in the IA-CS group completed the entire 24-week study period. At 24 weeks, a decrease in QUICK DASH score was observed in the IA-PRP group (16) compared to the IA-CS group (33). In terms of range of movement, the IA-PRP group showed significant improvement in abduction, internal rotation, and external rotation compared to the IA-CS group. No major complications were observed in any patients.
Conclusions: At the 24-week follow-up, a single dose of IA-PRP injection was found to be more effective than an IA-CS injection in improving pain, disability, and shoulder range of motion in patients with adhesive capsulitis of the shoulder.

Keywords: Adhesive capsulitis; Platelet-rich plasma; Corticosteroid; Intra-articular.

1. Introduction

One of the common causes of shoulder pain and upper extremity impairment is adhesive capsulitis (AC), which limits the glenohumeral (GH) joint's abilities, restricting both active and passive shoulder movements [1]. The limitation of the shoulder's passive range of motion (ROM), notably abduction and external rotation, is crucial to the clinical diagnosis of AC. In the general population, the prevalence of AC ranges from 2% to 5%, but it can reach 20% in diabetic patients [1]. The goal of AC treatment is to relieve discomfort, restore movement, and ultimately regain shoulder function. Intra-articular corticosteroid (IA-CS) injection, due to its affordability and patient acceptance, is still among the most commonly used methods of treating AC [1,2]. According to studies, IA-CS injection into the shoulder joint relieves symptoms and prevents the growth of capsular fibrosis [1,2]. However, IA-CS injection has been associated with hyperglycemia, negative effects on articular cartilage, an elevated risk of tendon rupture, localized skin depigmentation, and subcutaneous tissue atrophy [3]. Given the potential negative effects of IA-CS injection, it is crucial for both doctors and patients to understand how to create the best treatment plan for patients with AC who are ineligible for or unwilling to receive IA-CS injection.

Recent studies have shown that platelet-rich plasma (PRP) injections are beneficial in treating chronic tendon and muscle injuries, tendinopathies, osteoarthritis, and other conditions [4–11]. PRP therapy involves the concentration and subsequent reinjection of autologous "platelets" obtained by whole-blood centrifugation. PRP is safe for injection and possesses antinociceptive, anti-inflammatory, and regenerative characteristics,

according to studies. With chronic tissue injuries, platelet-rich plasma can speed up tissue repair while also reducing joint pain and stiffness [5–8,10,11]. However, there is not much evidence of its efficacy in AC patients.

This study aims to compare the effects of a single IA-PRP injection and a standard single IA-CS injection on pain and shoulder function in AC patients. We believe that reinjecting concentrated platelets may reduce synovial inflammation and speed up the natural repair of the joint capsule, leading to better pain and stiffness reduction in the shoulder joint of AC patients, in contrast to IA-CS injection.

2. Materials and Methods

2.1. Study Venue

The study was conducted in the Department of Orthopaedics at a tertiary teaching hospital.

2.2. Sample Size

The sample size was sixty (60) patients.

2.3. Study Period

The study was conducted from October 2020 to October 2022.

2.4. Data Collection

Data was collected from patients admitted to the Orthopaedic ward of the tertiary teaching hospital, with prior informed consent, using a proforma.

2.5. Inclusion Criteria

The following inclusion criteria were used for the study:

- Patients above 18 years of age of both genders,
- Pain for less than 12 months,
- Limitations of both active and passive movements of glenohumeral joint of less than or equal to 25% in at least two directions (abduction, external rotation, internal rotation, and flexion), as compared with the contralateral shoulder in the scapular plane and in progressive degree of horizontal adduction.

2.6. Exclusion Criteria

The following exclusion criteria were used for the study:

- Patients with concurrent bilateral shoulder pain,
- Uncontrolled diabetes mellitus,
- Overt hypothyroidism or hyperthyroidism,
- Patients who received any drug by intra-articular injection for treatment within 6 months prior to enrolment,
- History of shoulder trauma including dislocation, subluxation, and fracture,
- History of breast cancer or surgery around the shoulder, neck, and upper back,
- Neurological deficit,
- History of previous adverse reactions to corticosteroids,
- Secondary adhesive capsulitis, systemic inflammatory disease including rheumatoid arthritis, MRI evidence of rotator cuff injury.

2.7. Study Design

A prospective cohort study was conducted. Figure 1 shows a schematic diagram of the study. Sixty AC patients were enrolled in the study after giving their informed consent. In the test group (IA-PRP group), 30 patients received a single (2 ml) IA-PRP injection into the GH joint, while the control group (IA-CS group) received a single (2 ml) CS injection. PRP was administered to individuals with DM or a history of CS side effects, while CS injection was given to others. To create 2 ml of CS injection, 1 ml (40 mg) of triamcinolone acetonide and 1 ml of 2% lignocaine were mixed.

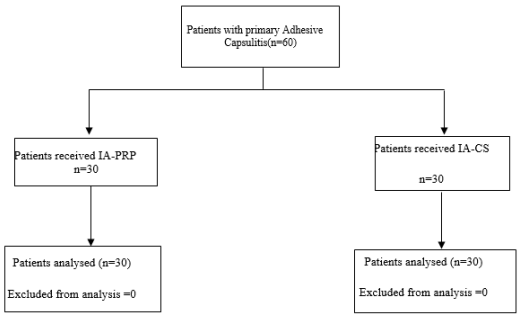


Figure 1. Flow diagram indicating the progress of participants through the study

2.8. Injection Protocol

Patients who met the inclusion criteria were alternately assigned to receive either platelet-rich plasma (PRP) or steroid injections. After providing a detailed description of the study, explaining the potential benefits and drawbacks of the intervention, and emphasizing the need for regular follow-up, informed consent was obtained from each patient. Patients in the PRP group provided fresh blood (approximately 28 ml), which was then mixed with an anticoagulant (2 ml). The blood was then centrifuged at 2500 and 3500 rpm for approximately ten and fifteen minutes, respectively, to produce 2 ml of PRP. Pre- and post-injection scores were recorded for each patient.

2.9. Injection Technique

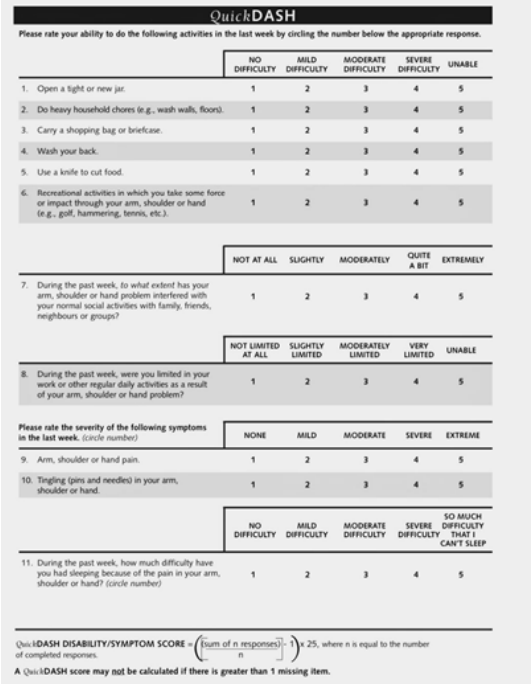
An interventional radiologist used a transducer to administer each injection. The posterior route was used for intra-articular injection into the Glenohumeral joint [12,13]. Patients were seated upright with their hands resting on their thighs. A 20-gauge needle was inserted semi-obliquely and parallel to the ultrasound probe to access the Glenohumeral joint. The expansion of the articular capsule was monitored during injection of the fluid (PRP or steroid). All injections were administered under aseptic conditions.

2.10. Post-Injection Protocol

Patients were instructed to avoid overhead and rotatory shoulder movements for the first two days following the injection. They were also given a detailed home exercise program to improve range of motion (ROM), which included wall-climbing exercises, Codman exercises [14], and stretches for the posterior and inferior shoulders. Patients were instructed to perform these exercises twice daily for thirty minutes, starting two days after the injection. NSAIDs were not allowed during the twelve-week observation period. Patients were permitted to take up to 1300 mg of acetaminophen (650 mg) daily for severe pain or discomfort. All patients were instructed to stop taking any medication 48 hours before their follow-up appointment. Patients were strongly encouraged to keep a notebook documenting their exercise frequency, duration, any challenges they encountered, and when they took their medication. The notebooks were reviewed at each subsequent session, and patients were contacted to remind them not to use any additional medications or physical agents and to encourage them to continue exercising.

2.11. Outcome Measures

A self-report questionnaire was used to assess the patient's clinical outcome at each review interval. The severity of adhesive capsulitis prior to injection was evaluated using a quick version of Disabilities of the Arm, Shoulder, and Hand (Quick DASH), as shown in Figure 2. Baseline characteristics were collected from all patients. Follow-up on the condition's outcome was performed using the same score at 4, 8, 12, and 24 weeks after the administration of either a single dose of Platelet Rich Plasma injection or a single dose of Corticosteroid injection and was examined with the aid of a pre-designed proforma.



QuickDASH

Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. Open a tight or new jar.	1	2	3	4	5
2. Do heavy household chores (e.g., wash walls, floors).	1	2	3	4	5
3. Carry a shopping bag or briefcase.	1	2	3	4	5
4. Wash your back.	1	2	3	4	5
5. Use a knife to cut food.	1	2	3	4	5
6. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).	1	2	3	4	5

	NOT AT ALL	SLIGHTLY	MODERATELY	QUITE A BIT	EXTREMELY
7. During the past week, *to what extent* has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups?	1	2	3	4	5

	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
8. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem?	1	2	3	4	5

Please rate the severity of the following symptoms in the last week. *(circle number)*	NONE	MILD	MODERATE	SEVERE	EXTREME
9. Arm, shoulder or hand pain.	1	2	3	4	5
10. Tingling (pins and needles) in your arm, shoulder or hand.	1	2	3	4	5

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
11. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? *(circle number)*	1	2	3	4	5

QuickDASH DISABILITY/SYMPTOM SCORE = $\left(\left[\frac{\text{sum of n responses}}{n}\right] - 1\right) \times 25$, where n is equal to the number of completed responses.

A QuickDASH score may not be calculated if there is greater than 1 missing item.

Figure 2. Quick DASH SCORE

2.12. Statistical Analysis

The required patient count was determined using power analysis software. The sample size was calculated with Quick DASH as the major outcome measure (pooled standard deviation = 14, two-sided t-test = 0.05). This study was planned to have 80% power to detect a difference of 10 points improvement in Quick DASH scoring between the two groups. Each group needed 30 volunteers to do this. The SPSS program (Statistical Package of Social Sciences, Chicago, IL) Version 22.0 was used to conduct the statistical analyses. Continuous data were displayed as mean SD, and categorical data were expressed as a percentage or a proportion. The differences in the changes of all parameters at various time periods were compared using repeated-measure analysis of variance. To compare the changes in various parameters from the baseline to the second, third, fourth, and fifth visits, a multivariate repeated ANOVA test was performed. In all tests, a P value of 0.05 or lower was regarded as statistically significant.

3. Results

3.1. Clinical Characteristics of the Patients

Sixty subjects were recruited in this study. Patients with adhesive capsulitis who matched the required criteria within the aforementioned time frame were included in the study (n=60). There were 33 males with 20 right-sided adhesive capsulitis and 13 left-sided adhesive capsulitis, and 27 females with 15 right-sided adhesive capsulitis and 12 left-sided adhesive capsulitis. The average age was 43.4 years (range: 30-67 years), and the typical time of symptoms was 7.5 months. All relevant data were analyzed. The average Quick DASH scores in both the platelet-rich plasma and steroid groups at pre-injection, 4 weeks, 8 weeks, 12 weeks, and 24 weeks post-injection are shown in the Table 1.

From the Figure 3, it is clear that the steroid group had a steep curve than the PRP group indicating the faster relief of pain initially. But by the end of the 24 weeks follow up the steroid group shows a flat curve pattern whereas the platelet-rich plasma group shows a falling curve pattern.

In this study, the QUICK DASH score in the platelet-rich plasma group is decreased from 84 to 16 at 24 weeks, when compared to the pre-injection score. Whereas the QUICK DASH score in the steroid group is decreased from 86 to 33 at 24 weeks, when compared to the pre-injection score.

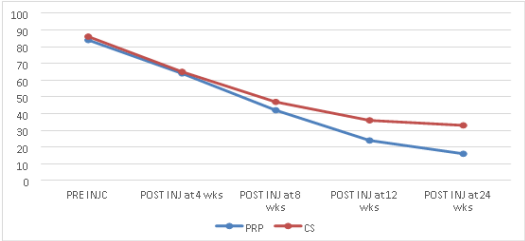


Figure 3. Quick dash comparison between PRP and steroid group

Table 1. Quick dash score comparison between PRP and steroid groups

Follow-up	Quick dash score (PRP group)	Quick dash score (Steroid group)
Pre-inj.	84	86
Post inj. 4 weeks	64	65
Post inj. 8 weeks	42	47
Post inj. 12 weeks	24	36
Post inj. 24 weeks	16	33

3.2. Paired sample statistics of PRP group

The paired sample test (p-value) in the PRP group between pre-injection and post-injection quick dash scores at 4, 8, 12, and 24 weeks showed strong significance. According to these statistical reports, the Quick DASH scores of patients gradually decrease when Platelet-rich plasma is administered, as shown in Table 2.

Table 2. Comparison between quick dash score means of pre- injection and 4,8,12,24 weeks respectively in PRP group only

		N	Mean	Std. Deviation	Mean differences	Standard deviation of mean differences	P value
Pair 1	PRE INJ	30	83.83	6.968	19.867	.730	.003
	Week 4	30	63.97	6.891			
Pair 2	PRE INJ	30	83.83	6.868	41.800	.805	<.001
	Week 8	30	42.03	6.790			
Pair 3	PRE INJ	30	83.83	6.968	59.933	1.112	<0.001
	Week 12	30	23.90	6.689			
Pair 4	PRE INJ	30	83.83	6.968	67.933	1.112	<0.001
	Week 24	30	15.90	6.789			

3.3. Paired Sample Statistics of CS Group

The paired sample test (p-value) in the CS group between pre-injection and post-injection 4, 8, 12, and 24 weeks Quick DASH scores respectively showed a strong significance. According to these statistical reports, the patient Quick DASH scores are decreasing gradually when corticosteroid is given, as shown in Tables 3-5.

To compare the Quick DASH scores of PRP and CS patient groups, a statistical t-test was conducted. The p-value was found to be insignificant at the 4th week, but it became more significant at the 24th week, as shown in Table 6.

Table 3. Comparison between quick dash score means of pre-injection and 4,8,12,24 weeks respectively in CS group only

		N	Mean	Std. Deviation	Mean differences	Standard deviation of mean differences	P value
Pair 1	PRE INJ	30	86.17	6.613	20.900	.305	.004
	Week 4	30	65.27	6.560			
Pair 2	PRE INJ	30	86.17	6.613	39.033	.615	.003
	Week 8	30	47.13	6.522			
Pair 3	PRE INJ	30	86.17	6.613	50.300	1.860	<0.001
	Week 12	30	35.87	6.684			
Pair 4	PRE INJ	30	86.17	6.613	54.267	3.290	<0.001
	Week 24	30	31.90	6.472			

Table 4. Paired sample tests between PRP & CS groups

Group Statistics				
	Group	N	Mean	Standard Deviation
Preinjection	PRP	30	83.83	6.968
	CS	30	86.17	6.613
4 Weeks	PRP	30	63.97	6.891
	CS	30	65.27	6.560
8 Weeks	PRP	30	42.03	6.790
	CS	30	47.13	6.522
12 Weeks	PRP	30	23.90	6.789
	CS	30	35.87	6.684
24 Weeks	PRP	30	15.90	6.789
	CS	30	31.90	6.472

Table 5. T test between PRP & CS group in respective weeks

T test for quality of means		P values
Pre-injection	Equal variances assumed	.189
4 Weeks	Equal variances assumed	.457
8 Weeks	Equal variances assumed	.004
12 Weeks	Equal variances assumed	<0.001
24 Weeks	Equal variances assumed	<0.001

Table 6. Multivariate repeated ANOVA test

Multivariate ANOVA Tests		
Effect		P value
Factor 1	Pillai's Trace	<0.001
	Wilks' Lambda	<0.001
	Hotelling's Trace	<0.001
	Roy's Largest Root	<0.001
	Mauchly's Test of Sphericity	<0.001

4. Discussion

The results of the study indicate that both Platelet Rich Plasma and Corticosteroids are effective in improving the range of motion (R.O.M) and providing pain relief for up to 6 months. However, after conducting a comparative T-test, the statistics in the 4th week show that corticosteroids provide better pain relief and R.O.M improvement (p-value - 0.457). Subsequently, after continuous follow-up of 8, 12, and 24 weeks, greater improvement is observed in patients treated with PRP than CS (p-value < 0.001). Multivariate

repeated ANOVA tests of different factors also have a p-value of less than 0.001, indicating the strong significance of the study, see Figures 4 and 5.

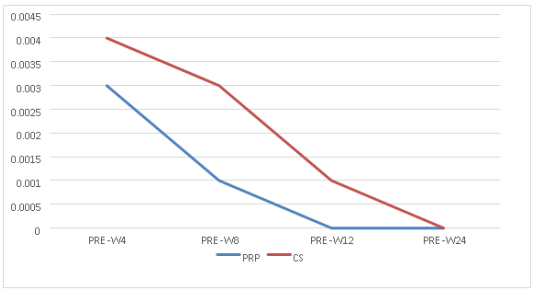


Figure 4. Line diagram of P values of PRP & CS group

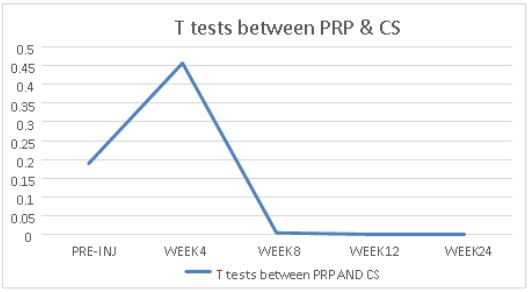


Figure 5. T test between PRP & CS groups

There by comparing the efficacy of PRP & CS injections in the treatment of Adhesive Capsulitis, at 24 weeks intra-articular PRP injection provided good pain relief and better functional improvement than Corticosteroid injection. The intra-articular PRP group improved shoulder ROM significantly as well. Both groups experienced a significant reduction in pain within the first four weeks of intervention. At 4th week, Corticosteroid group is more statistically significant. But at the end of 24 weeks, the PRP group showed significant improvement in Quick DASH score. Patients in the PRP group consumed less acetaminophen, which indirectly confirmed that the PRP group experienced better pain relief than the CS groups. Patients who received PRP injections reported higher levels of treatment satisfaction.

In 2017, Kothari et al. observed similar trend in 190 patients, by giving a single dose of PRP injection resulted in significant improvement in shoulder R.O.M, pain & function ultrasonic therapy in 190 patients with A.C shoulder [15]. In 2018, Saif et al. [16] reported that intra-articular injections with both PRP and steroids are effective, non-surgically less invasive, and cost effective lines of treatment for mild-moderate shoulder osteoarthritis, with superiority to PRP in terms of long-term therapeutic effects compared to steroid injection [16]. In 2019, Havva Talay et al. proposed that PRP provides analgesia through its effects on cannabinoid receptors, in addition to a complex and unexplained mechanism of action associated with enriched growth factor content and a protein in platelet alpha granules, which initially induces a proinflammatory mechanism and then decreases inflammation and helps in treating adhesive capsulitis. In 2021, Barman et al. reported that PRP injections significantly improved shoulder pain & function in a diabetic population when compared to an institution-based physical training programme for shoulder AC [17].

The study's advantages included a clear definition of the conditions, enrollment of the entire population with adhesive capsulitis, ultrasound-guided injections, and analysis of functional outcomes at different time points. These factors all provided top-notch proof of the efficacy of PRP and CS injections as well as their effects over time. Patients enrolled from different groups had similar baseline characteristics; no statistically significant differences were discovered between study populations. All trial participants received intra-articular injections that were guided by ultrasonography. All of the treatments were carried out by a single operator who has experience providing ultrasound-guided intraarticular injections. Using capsular distension during the injection, the accuracy of an ultrasound-guided injection was assessed in real time.

Adhesive capsulitis is postulated to be an inflammatory and fibrotic condition. Corticosteroid injections have demonstrated an outcome for Adhesive capsulitis by reducing inflammation, which has resulted in improved clinical outcome [18]. PRP's detailed mechanism of action, on the other hand, is not well understood because it has both pro-inflammatory & anti-inflammatory properties. According to literature, PRP releases a variety of growth factors like platelet derived growth factor, transforming growth factor, vascular & epidermal endothelial growth factor [19–21], that are essential for tissue repair mechanism, but also a high amount of RANTES/ CCL5 (major monocyte chemo attractant factor) from its alpha granules [22]. RANTES/CCL5 is a C-C chemokine subfamily member that regulates leukocyte recruitment and diminishes inflammatory & nociceptive responses. RANTES/ CCL5 hinders the production of many cytokines by basophils and lowers concentration of A4 lipoxin (anti inflammatory marker), reducing the count of inflammatory cells. Aside from that, Platelet rich plasma produces hepatocyte growth factor & tumour necrosis factor, both of which have potent anti-inflammatory properties [23]. PRP's anti nociceptive effect probably due to cannabinoid receptor augmentation, specifically CB1 and CB2 [24].

Platelets concentration in platelet rich plasma primarily determines PRP quality [20].Because more platelets in PRP can result in a more significant clinical response [25]. Our method yielded a Mean Platelet count of 696 $\times$ 10^3/l. We obtained a greater than four times increase in the number of platelets in PRP, which was previously considered a standard and effective count. Leucocytes presence in PRP and their impact on the clinical effectiveness of platelets are highly controversial. Leucocytes can trigger an inflammatory response, and while some studies have advised against using them in PRP because of this, others also have indicated that leucocytes have positive effects like antimicrobial and immunological resistance [26,27]. As previously stated, PRP was prepared in this study using a double centrifugation technique. Our PRP product's mean leucocyte concentration, which ranged from 0.1 to 1.5$\times$$10^3$/l, was thus far lower than that of the standardised leucocyte reduced blood product [27].

The fact that PRP may have significant benefits on all stages of tissue healing, including the inflammatory, proliferative & remodelling phases of capsular repair in Adhesive Capsulitis, may help to explain why PRP patients in our study experienced greater improvements. PRP most likely altered synovial fluid cytokine levels and decreased synovial membrane hyperplasia more efficiently than CS, leading to improved shoulder pain alleviation. Patients may have performed home exercises more properly, leading to a temporary improvement in overall clinical outcome, because pain dropped dramatically and overall joint. These explanations are based on scientifically informed suspicions rather than data from this study, which did not investigate the molecular basis of PRP's action on capsular healing. More research is needed, however, to confirm the findings and understand the detailed mechanisms by which PRP works, as well as to determine whether the improvement is only temporary or if PRP plays a more important role through disease-modifying properties [22].

When the results of this study are compared to the results of six-month follow-up, the result for the CS group is reduced. whereas the PRP group's outcome is preserved. The platelet-rich plasma group had higher pre-injection Quick DASH scores and lower after 24 weeks, which was a significant finding. This adds to our belief that platelet-rich plasma injection is superior to corticosteroid injection [25]. Uniform administration of PRP and corticosteroids in alternative patients, Small sample size are Limitations for this study. Proper randomisation of the patient groups, Use of large sample size, Increase of follow-up period are the recommendations for further studies.

5. Conclusion

In conclusion, the comparative study of management of adhesive capsulitis with platelet-rich plasma vs corticosteroid injection shows that a single dose of Platelet-rich plasma injection improves shoulder pain and functional activities more efficiently than injecting single dose Corticosteroid into the Adhesive Capsulitis. These improvements were maintained over in our follow-up period without any significant complications. Corticosteroid gives better results up to the Fourth week and after that, the effect decreased slightly. Long-term follow-up with a larger number of patients is required to assess the long-term benefits of pain relief & functional improvement in adhesive capsulitis.

Author Contributions: All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

References

[1] Koh, K. H. (2016). Corticosteroid injection for adhesive capsulitis in primary care: a systematic review of randomised clinical trials. Singapore Medical Journal, 57, 646-657.

[2] Chang, K. V., Wu, W. T., Han, D. S., et al. (2017). Static and dynamic shoulder imaging to predict initial effectiveness and recurrence after ultrasound-guided subacromial corticosteroid injections. Archives of Physical Medicine and Rehabilitation, 98, 1984-1994.

[3] Waterbrook, A. L., Balcik, B. J., & Goshinska, A. J. (2017). Blood glucose levels after local musculoskeletal steroid injections in patients with diabetes mellitus: a clinical review. Sports Health, 9, 372-374.

[4] Patel, S., Dhillon, M. S., Aggarwal, S., et al. (2013). Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. American Journal of Sports Medicine, 41, 356-364.

[5] Kothari, S. Y., Srikumar, V., & Singh, N. (2017). Comparative efficacy of platelet rich plasma injection, corticosteroid injection and ultrasonic therapy in the treatment of periarthritis shoulder. Journal of Clinical and Diagnostic Research, 11, RC15-RC18.

[6] Dai, W. L., Zhou, A. G., Zhang, H., & Zhang, J. (2017). Efficacy of platelet-rich plasma in the treatment of knee osteoarthritis: a meta-analysis of randomized controlled trials. Arthroscopy: The Journal of Arthroscopic and Related Surgery, 33, 659-670.e1.

[7] Jang, S. J., Kim, J. D., & Cha, S. S. (2013). Platelet-rich plasma (PRP) injections as an effective treatment for early osteoarthritis. European Journal of Orthopaedic Surgery & Traumatology, 23, 573-580.

[8] Mishra, A., & Pavelko, T. (2006). Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. American Journal of Sports Medicine, 34, 1774-1778.

[9] Aslani, H., Nourbakhsh, S. T., Zafarani, Z., Ebrahimi, I., & Abbaszadeh, M. (2016). Platelet-rich plasma for frozen shoulder: a case report. Archives of Bone and Joint Surgery, 4(1), 90-93.

[10] Filardo, G., Kon, E., Di Matteo, B., Di Martino, A., Tesei, G., Pelotti, P., & Marcacci, M. (2014). Platelet-rich plasma injections for the treatment of refractory Achilles tendinopathy: results at 4 years. Blood Transfusion, 12(4), 533-540.

[11] Descalzi, F., Ulivi, V., Cancedda, R., & Piscitelli, F. (2013). Platelet-rich plasma exerts antinociceptive activity by a peripheral endocannabinoid-related mechanism. Tissue Engineering Part A, 19(19-20), 2120-2129.

[12] Chen, C. P., Lew, H. L., & Hsu, C. C. (2015). Ultrasound-guided glenohumeral joint injection using the posterior approach. American Journal of Physical Medicine & Rehabilitation, 94(10), e117-e118.

[13] Lee, D. H., Yoon, S. H., Lee, M. Y., Kwack, K. S., Rah, U. W., & Lim, H. C. (2017). Capsule-preserving hydrodilatation with corticosteroid versus corticosteroid injection alone in refractory adhesive capsulitis of shoulder: a randomized controlled trial. Archives of Physical Medicine and Rehabilitation, 98(5), 815-821.

[14] Kumar, S. (2019). Comparative analysis on efficacy of injection methyl prednisolone vs Autologous PRP in Adhesive Capsulitis peri Arthritis – Frozen shoulder. International Journal of Medical Research & Health Professions, 5(4), 278-281.

[15] Kothari, S. Y., Srikumar, V., & Singh, N. (2017). Comparative efficacy of platelet-rich plasma injection, corticosteroid injection and ultrasonic therapy in the treatment of periarthritis shoulder. Journal of Clinical and Diagnostic Research, 11(5), RC15-RC18.

[16] Saif, D. S., Serag, D. M., & El Tabl, M. A. (2019). Comparative study between platelet-rich plasma injection and steroid injection in mild-moderate shoulder osteoarthritis and their relation to quality of life. Egypt Rheumatol Rehabil, 46, 55-61.

[17] Barman, A., Mukherjee, S., Sinha, M. K., Sahoo, J., & Viswanath, A. (2021). The benefit of platelet-rich plasma injection over institution-based physical therapy program in adhesive capsulitis patients with diabetes mellitus: Prospective observational cohort study. Clinical Shoulder and Elbow, 24(4), 215-223.

[18] Aslani, H., Nourbakhsh, S. T., Zafarani, Z., et al. (2016). Platelet-rich plasma for frozen shoulder: A case report. Archives of Bone and Joint Surgery, 4, 90-93.

[19] Kesikburun, S., Tan, A. K., Yilmaz, B., et al. (2013). Platelet-rich plasma injections in the treatment of chronic rotator cuff tendinopathy: A randomized controlled trial with 1-year follow-up. American Journal of Sports Medicine, 41, 2609-2616.

[20] Gautam, V. K., Verma, S., Batra, S., et al. (2015). Platelet-rich plasma versus corticosteroid injection for recalcitrant lateral epicondylitis: Clinical and ultrasonographic evaluation. Journal of Orthopaedic Surgery, 23, 1-5.

[21] Abdul Ameer, L. A., Raheem, Z. J., Abdulrazaq, S. S., et al. (2018). The anti-inflammatory effect of the platelet-rich plasma in the periodontal pocket. European Journal of Dentistry, 12, 528-531.

[22] Bendinelli, P., Matteucci, E., Dogliotti, G., et al. (2010). Molecular basis of anti-inflammatory action of platelet-rich plasma on human chondrocytes: Mechanisms of NF-$\kappa\beta$ inhibition via HGF. Journal of Cellular Physiology, 225, 757-766.

[23] Lee, H. R., Park, K. M., Joung, Y. K., et al. (2012). Platelet-rich plasma loaded hydrogel scaffold enhances chondrogenic differentiation and maturation with upregulation of CB1 and CB2. Journal of Controlled Release, 159, 332-337.

[24] Arora, S., & Agnihotri, N. (2017). Platelet derived biomaterials for therapeutic use: Review of technical aspects. Indian Journal of Hematology and Blood Transfusion, 33, 159-167.

[25] Moojen, D. J., Everts, P. A., Schure, R-M., et al. (2008). Antimicrobial activity of platelet-leukocyte gel against Staphylococcus aureus. Journal of Orthopaedic Research, 26, 404-410.

[26] Mazzocca, A. D., McCarthy, M. B., Chowaniec, D. M., et al. (2012). Platelet-rich plasma differs according to preparation method and human variability. Journal of Bone and Joint Surgery, 94, 308-316.

[27] Sharma, R. R., & Marwaha, N. (2010). Leuko reduced blood components: Advantages and strategies for its implementation in developing countries. Asian Journal of Transfusion Science, 4(1), 3-8.